Remarks

In compliance with requests by the Examiner (discussed further below), Applicants have amended claim 54 to correct a grammatical error, amended the title to more clearly indicate the invention to which the claims are directed, and amended the specification to update the priority information. Claims 76-85 have been added to claim additional embodiments that Applicants regard as the invention. The new claims are supported by the specification as filed.

More particularly, support for new independent claim 76 can be found, for example, at Table I, page 327, row 3 as indicated as "Gene No. 62"; and page 389, lines 11-17 (protein expressed on the surface of a cell).

Upon entry of the present amendment, claims 1-85 are pending in the application. No new matter has been added.

Formal Matters

The Examiner has noted that "the lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors." *See*, Paper No. 20040503, page 2, paragraph 2(a). In response, Applicants submit that they have corrected errors in the specification of which they are aware and note that they will correct any errors which they become aware of. Therefore, it is respectfully requested that the objection to the specification be withdrawn.

The Examiner has "requested that the Applicant update the priority information in the first line of the specification with the patent number for USSN 09/205,258." *See*, Paper No. 20040503, page 2, paragraph 2(b). Applicants note that the priority has been updated thereby obviating the instant objection. Thus, Applicants respectfully request that the objection to the specification regarding the priority information be withdrawn.

A new title that is "more clearly indicative of the invention to which the claims are directed" has also been requested by the Examiner. *See*, Paper No. 20040503, page 2, paragraph 2(c). In respect of this request, Applicants have herein amended the title to recite: "SECRETED PROTEIN HEMAE80 ANTIBODIES." Therefore, Applicants respectfully request that the objection to the title be withdrawn.

Claim 54 was objected to because "[c]laim 54 (part d) recites 'amino acid residues the polypeptide', which is missing the word 'of' between 'residues' and 'the'." *See*, Paper No.

20040503, page 2, paragraph 3. Applicants have herein amended claim 54 to correct the grammatical error. Therefore, it is respectfully requested that the objection to claim 54 be reconsidered and withdrawn.

Rejections under 35 U.S.C. §§ 101 and 112, First Paragraph

The Examiner has rejected claims 1-75 because the invention is allegedly not supported by a specific and substantial asserted utility or a well-established utility. *See,* Paper No. 20040503, page 3, paragraph 5. More particularly, the Examiner alleges that:

> based on the expression of the gene encoding the polypeptide of SEQ ID NO:310 and not the expression of the polypeptide of SEQ ID NO:310, the specification generally asserts that the disclosed polypeptide of SEQ ID NO:310 *may be useful* for a number of purposes; however, none of these asserted uses meet the 'specific' and 'substantial' utility requirements of 35 U.S.C. § 101." (emphasis added in original)

Id. at page 4. Furthermore, the Examiner concludes that:

> the specification does not support a specific and substantial asserted utility or a well-established utility regarding the claimed antibodies because the polypeptide (i.e., SEQ ID NO:310) to which the antibodies bind does not have a specific and substantial asserted utility or a well-established utility.

Id. at page 7, first full paragraph.

Applicants respectfully disagree and traverse this rejection.

Applicants point out that the Federal Circuit has held that "[w]hen a properly claimed invention meets at least one stated objective, utility under 35 U.S.C. § 101 is clearly shown." *Raytheon v. Roper*, 724 F.2d 951, 958 (Fed. Cir. 1983). Accordingly, the specification does, in fact, provide a specific and substantial utility for the HEMAE80 polypeptide and, therefore, also provides a specific utility for the antibodies as tumor markers or immunotherapy targets. *See*, page 99, lines 23-24. First, the specification teaches that "the protein product of this gene is useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia" where an insufficient number of hematopoietic cells contributes to the diseases and where bone marrow transplantation and/or reconstitution can be used to treat such diseases. *See,* page 99, lines 7-11. Second, the specification teaches that "this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types." *See*, page 99, lines 15-17. Therefore, the specification clearly asserts a specific use for the polypeptides in

regulating the production of cells of hematopoietic lineages and correlates this biological function to the specific hematopoietic related disorders cited above.

Additionally, Applicants have submitted post-filing date publications which *further corroborate* the specific and substantial utilities described in the specification[1]. For example, Liu *et al.*, "Molecular Cloning and Chromosomal Mapping of a Candidate Cytokine Gene Selectively Expressed in Human CD34+ Cells", Genomics (2000) 65:283-292 (cited as Reference AD, in Applicants' Information Disclosure Statement of December 20, 2001) identify a secreted protein (referred to as C17) which is preferentially expressed in a rare population of CD34+ hematopoietic stem/progenitor cells in human bone marrow and neonatal cord blood. *See* Liu *et al.* (2000) page 283, first column. Applicants point out that the C17 polypeptide sequence is identical to the HEMAE80 polypeptide sequence. Moreover, data from Liu *et al.* discloses that when bone marrow CD34+ hematopoietic stem/progenitor cells were treated with known hematopoietic cytokines under conditions favorable to the maintenance and proliferation of stem/progenitor cells, C17 expression was elevated. *See Id.* at page 286, second column to page 287, second column, and Figure 3. Conversely, when bone marrow CD34+ cells were treated with hematopoietic colony stimulating factors resulting in hematopoietic differentiation and CD34+ cell reduction, C17 expression was reduced. *See Id.*

Additional support can be found in two International Applications published after the priority date of the present application. WO 00/56889 (submitted as Reference AA in Applicants' Information Disclosure Statement of December 20, 2001) and WO 02/00690 (relevant parts submitted herewith as Reference AZ in a supplemental IDS) demonstrate that HEMAE80 (referred to as PRO4425 in both applications; see alignment submitted herewith as Exhibit A) can induce proliferation of kidney mesangial and umbilical vein endothelial cells, respectively. *See* WO 00/56889, example 41 and WO 02/00690, example 21. Applicants note that it was well-known in the art that kidney mesangial cells are used to test for cell proliferative activity as these cells are known to be responsive to proliferative cytokines. *See* Makino *et al.*, (2000) Nephrol Dial Transplant 15:1140, 1140 (submitted herewith as Exhibit B and as Reference BA in a supplemental IDS). Furthermore, it was also

[1] Applicants note that supportive data in third party publications, dated after the applicants' priority date, "can be used to substantiate any doubts as to asserted utility since it pertains to the accuracy of a statement already in the specification." *See e.g., In re Brana* 51 F.3d 1560, 1567 at n19 (Fed. Cir. 1995).

well-known that human umbilical vein endothelial cells are used to test for possible growth factor functions, as discussed in example 21 of WO 02/00690.

These data from post-priority date references corroborate Applicants asserted utility that the polypeptides of the invention may be useful in cell proliferation and differentiation, particularly of hematopoietic stem cells. *See* page 99, lines 15-17 of the specification. Furthermore, Applicants note that it was well known in the art that hematopoietic stem cells were pluripotent, *i.e.*, capable of self-renewal as well as giving rise to red blood cells, white blood cells, and immunocompetent cells. *See*, Alberts *et al.*, Molecular Biology of the Cell, 3rd edition, pages 1162-1169 (1994); Gilbert, S., Developmental Biology, 3rd edition, pages 229-237 (1991). Consequently, a protein that regulates hematopoiesis will effect many immune cell related diseases and disorders, and the mere fact that the protein effects many different activities does not render these activities non-specific or insubstantial. Thus, given the disclosure in the specification and the support from post filing-date reference, one of ordinary skill in the art would, more likely that not, conclude that Applicants' asserted utility is specific.

Applicants note that the test for specificity is whether an asserted utility is specific to the subject matter claimed, in contrast to a utility that would be applicable to the broad class of the invention. *See* M.P.E.P § 2107.01 on page 2100-32. All that is required of Applicants is that there be a reasonable correlation between the biological activity and the asserted utility. *See Nelson v. Bowler*, 626 F.2d 853, 857 (C.C.P.A. 1980) (emphasis added). Accordingly, the disclosed utility for the protein HEMAE80 discussed above is specific, in that not every protein is useful for the diagnosis and/or treatment of the above-mentioned hematopoietic diseases.

Furthermore, the Examiner alleges that the claimed invention is not supported by a substantial utility. As discussed above, Applicants assert that based on what is disclosed in the specification, coupled with what was known in the art on the earliest effective priority date of the present invention, it is reasonable that the claimed invention is useful in the diagnosis and/or treatment of certain hematopoietic disorders, and that such uses fulfill an unmet medical need. The M.P.E.P. states, "any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a 'substantial' utility." *See* M.P.E.P. § 2107.01(I). Applicants thus assert the claimed invention is supported by a substantial or "real world" utility.

In view of the above arguments, Applicants have provided evidence and reasoning which supports the Applicants' assertion of a patentable utility. The utilities asserted in the specification for Secreted Protein HEMAE80 are specific, substantial and well-established. Accordingly, Applicants respectfully submit that the rejection of claims 1-75 under 35 U.S.C. § 101 has been obviated. Therefore, Applicants respectfully request that the rejection be reconsidered and withdrawn.

For the reasons discussed above in response to the rejection under 35 U.S.C. § 101, the claimed invention is supported by a specific, substantial and well-established utility. Therefore, the Examiner "should not impose a 35 U.S.C. § 112, first paragraph, rejection grounded on a 'lack of utility' basis unless a 35 U.S.C. §101 rejection is proper." M.P.E.P. § 2107 (IV) at 2100-36. Since the claimed invention complies with the utility requirement of 35 U.S.C. § 101, the rejection of claims 1-75 under 35 U.S.C. § 112, first paragraph, based on the alleged lack of utility of the claimed invention, should be withdrawn. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Indefiniteness Rejections under 35 U.S.C. § 112, Second Paragraph

A. Claims 16, 37, 53, and 75

Claims 16, 37, 53 and 75 have been rejected under 35 U.S.C. § 112, second paragraph for alleged indefiniteness. In particular, the Examiner alleges that it is unclear whether "the hybridoma produce an antibody fragment or does the hybridoma produce the antibody from which an antibody fragment can be produced." See Paper No. 20040505, page 8, paragraph 8(a).

Applicants respectfully disagree and maintain that claims 16, 37, 53 and 75, as previously pending, complied with 35 U.S.C. § 112, second paragraph. However, Applicants have amended claims 16, 37, 53 and 75 to omit the phrase "or fragment thereof," thereby obviating the instant rejection. Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 16, 37, 53, and 75 for alleged lack of indefiniteness.

B. Claims 38-75

Claims 38-75 have been rejected under 35 U.S.C. § 112, second paragraph for alleged indefiniteness. In particular, the Examiner asserts that "it is unclear if the HEMAE80 cDNA

contained in ATCC Deposit No. 97975 encodes the secreted polypeptide and the full-length polypeptide." See Paper No. 20040503, page 8, paragraph 8(b).

Preliminarily, Applicants point out that the Examiner incorrectly associates the cDNA contained in ATCC Deposit No. 97975 with clone HLHFP03. *See Id.* at page 8. Applicants note that clone HLHFP03 is contained in ATCC Deposit No. 209126 and is currently in prosecution in U.S. patent application Serial No: 09/984,490. Thus, Applicants will address the current indefinite rejection only as it pertains to clone HEMAE80.

Applicants respectfully disagree and traverse this rejection.

Initially, Applicants note that the HEMAE80 cDNA clone contained in ATCC Deposit No. 97975 is the full-length polynucleotide. Accordingly, both the full-length polypeptide and the mature (processed during expression) polypeptide are encoded by the HEMAE80 cDNA contained in ATCC Deposit No. 97975. Applicants point out that the mature and/or the secreted forms of the polypeptide are *inherent* to the full-length polypeptide sequence encoded by the HEMAE80 cDNA.

Applicants respectfully direct the Examiner's attention to M.P.E.P § 2163.07(a), which states that by "disclosing in a patent application a device that *inherently* performs a function or has a property, operates according to a theory or has an advantage, a *patent application necessarily discloses* that function, theory or advantage, even though it says nothing explicit concerning it" (emphasis added). Furthermore, the M.P.E.P. states that "where the invention involves a biological material and words alone cannot sufficiently describe how to make and use the invention in a reproducible manner, access to the biological material may be necessary for the satisfaction of the statutory requirements for patentability under 35 U.S.C. § 112." (M.P.E.P. § 2402).

Thus, Applicants submit that the recitation of the secreted protein and the full-length protein in connection with the cDNA contained in ATCC Deposit No. 97975 is inherent and fully disclosed and defined by the instant specification. Accordingly, Applicants respectfully request that the Examiner withdraw the rejection of claims 38-75 under 35 U.S.C. § 112, second paragraph.

C. Claims 6, 43, and 66

Claims 6, 43, and 66 have also been rejected under 35 U.S.C. § 112, second paragraph for alleged indefiniteness. Specifically, the Examiner alleges that "an antibody that is specific for protein (a) would not also be specific for protein (b), since an antibody specific

for protein (a) inherently binds an epitope within amino acid residues 1-24 of SEQ ID NO:310." *See* Paper No. 20040503, page 9, paragraph 8(c).

Applicants respectfully disagree and traverse.

Initially, Applicants note that those who ordinarily conducted research with antibodies at the time of the effective filing date understood that antibodies that "specifically bind" a particular protein might also be capable of binding that protein in a variety of forms. Therefore, depending on the presence or absence of a particular antigenic epitope, antibodies that specifically bind to a particular protein could also specifically bind to fragments or variants of the protein, such as orthologues, splice variants, and allelic variants (*i.e.*, polypeptides encoded by mutated from of the gene encoding a particular protein). Thus, the ability of an antibody to specifically bind a protein and fragments or variants of the protein would depend on the presence of the specific antigenic epitope to which the antibody binds.

In the present case, Applicants point out that independent claims 1, 38, and 61, of which claims 6, 43, and 66 depend on, respectively, are Markush claims directed to different portions of the HEMAE80 protein. Therefore, independent claim element (a) consisting of the full-length portion of the HEMAE80 protein and element (b) consisting of the mature portion of the HEMAE80 protein have many common specific antigenic epitopes to which specific antibodies bind. For example, epitopes in common for both the full-length and mature HEMAE80 protein might "include those comprising a sequence shown in SEQ ID NO:310 as residues: Ser-91 to Lys-98." *See,* page 99, lines 3-4 of the specification.

For the reasons discussed above, claims 6, 43, and 66 clearly set forth the subject matter which Applicants regard as their invention. Applicants assert that claims 6, 43, and 66 are directed to a subset of antibodies that specifically bind to both the full-length HEMAE80 protein and the mature HEMAE80 protein. Therefore, the antibodies encompassed by the claims that bind to both sequences do so by binding to antigenic epitopes of the full-length that are also conserved in the processed forms. Accordingly, it is respectfully requested that the rejection of claims 6, 43, and 66 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

Rejections Under 35 U.S.C. § 112, First Paragraph

A. Claims 1-75

The Examiner has rejected claims 1-75 under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. *See*, Paper No. 20040503, pages 9-13. More specifically, the Examiner alleges:

> undue experimentation would be required to practice the claimed antibodies in a diagnostic or therapeutic setting with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed invention and absent working examples providing evidence which is reasonably predictive that the claimed antibodies are effective for immunotherapy.

See, Paper No. 20040503, page 13, penultimate paragraph.

Applicants respectfully disagree and traverse.

In support of the enablement rejection, the Examiner refers to factors set forth in *Ex Parte Forman* (230 U.S.P.Q. 546 (1986)) that are to be considered in determining whether or not a specification is sufficiently enabling without undue experimentation. Applicants assert, however, that in contrast to the situation in *Ex Parte Forman*, the specification in the present case is sufficiently enabling to one having ordinary skill in the relevant field. Moreover, the present case is closely analogous to the situation presented and decided upon in *In Re Wands* (where the court affirmed and opined upon the eight considerations iterated in *Ex Parte Forman). See, In re Wands,* 858 F.2d 731 (1988). In this regard, the M.P.E.P. has also explicitly incorporated the decision in *In Re Wands* as part of the guidelines to be utilized in considering enablement issues:

> *In re Wands,* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (reversing the PTO's determination that claims directed to methods for detection of hepatitis B surface antigens did not satisfy the enablement requirement). In *Wands*, the Court noted that there was no disagreement as to the facts, but merely a disagreement as to the interpretation of the data and the conclusion to be made from the facts. *In re Wands,* 858 F.2d at 736-40, 8 USPQ2d at 1403-07. The Court held that the specification was enabling with respect to the claims at issue and found that "there was considerable direction and guidance" in the specification; there was "a high level of skill in the art at the time the application was filed;" and "all of the methods needed to practice the invention were well known." 858 F.2d at 740, 8 USPQ2d at 1406. After considering all the factors related to the enablement issue, the court concluded that "it would not require undue experimentation to obtain antibodies needed to practice the claimed invention." *Id.*, 8 USPQ2d at 1407.

M.P.E.P., 8th Ed., § 2164.01(a) (Aug. 2001, *revised* Feb. 2003) (emphasis added).

The present application presents a situation very much like that considered in *In Re Wands* where the specification was found enabling for the claimed antibodies because of the considerable direction and guidance in the specification, the high level of skill in the art, and the well-established methods needed to practice the invention. As discussed below, the present specification does, like *In Re Wands*, provide more than ample guidance to those of ordinary skill in the art for how to make and use the claimed antibodies and methods based thereon.

Furthermore, the legal standard for evaluating enablement, as cast by the C.C.P.A. and the Federal Circuit, is whether the antibodies encompassed by the claims have at least a single use, and this use can be confirmed, without undue experimentation, by following procedures either described in the specification or otherwise known in the art. See, *In re Angstadt*, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976). According to the M.P.E.P. §2164.01 (b), "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied." Citing *In re Fisher*, 427, F.2d 833, 839 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970).

As of June 6, 1997 (the claimed priority date for the present application), and as pointed out in the present application, methods for making and using a diverse array of antibody types (*e.g.* monoclonal, single-chain, Fab fragments, etc.) were routine for those of ordinary skill in the art. *See e.g.*, specification, page 373, line 35, to page 374 line 21. In this regard, the specification describes various types of antibodies that may be produced against the protein of SEQ ID NO: 310. The specification also describes how to produce an antibody from the protein of SEQ ID NO: 310. *See, e.g.*, specification, Example 10, page 410, line 34, to page 412, line 15. The specification also describes and details examples of assays that may be used, such as radioimmunoassays, competitive-binding assays, Western blot analysis, ELISA assays, and describes how antibodies may be used to carry out *in vivo* imaging. *See*, specification at pages 381, line 5, to page 382, line 26. Hence, Applicants submit that the present application provides sufficiently ample guidance as of its original priority date in teaching how to make and use the presently claimed antibodies and methods based thereon.

Additionally, the Examiner alleges that the specification does not enable the use of the claimed antibodies because:

> [w]hat the specification does not do is teach the expression of the protein of SEQ ID NO:310 in any specific tissue nor does the specification correlate the expression of SEQ ID NO:310 with any particular disease state and the specification does not teach whether SEQ ID NO:310 would be overexpressed or underexpressed in a particular disease state such that an antibody, which specifically binds SEQ ID NO:310 would be useful for immunotherapy

and

> [t]hose of skill in the art recognize that expression of mRNA (i.e., gene expression), specific for a tissue type, does not necessarily correlate nor predict equivalent levels of polypeptide expression.

See, Paper No. 20040503, page 11. In support of the Examiner's allegations, publications were cited to illustrate that there is not always a direct correlation between mRNA and protein expression levels. *See*, Paper No. 200400503, pages 11-12.

Applicants respectfully disagree and assert that although it is true that mRNA expression levels do not always exhibit a direct proportional correlation with protein expression levels, the lack of at least some general connection is the exception rather than the norm. Indeed, the comments in Fu *et al.*, Powell *et al.*, Lewin *et al.*, and Jang *et al.* were in fact worthy of publication precisely because they represent exceptions to the norm, not because they are paradigms of the norm. Furthermore, in contrast to the references relied upon by the Examiner, Alberts *et al.* teaches, "For most genes transcriptional controls are paramount. This makes sense because of all the possible control points...only transcriptional control ensures that no superfluous intermediates are synthesized." *See*, Alberts *et al.*, Molecular Biology of the Cell, 3rd edition, page 405, last paragraph (1994) (Reiterated in the Summary paragraph, page 404; "Although all of the steps involved in expressing a gene can in principle be regulated, for most genes the initiation of RNA transcription is the most important point of control.") (Emphasis added). Hence, when investigating the expression levels of a new gene and protein those of ordinary skill in the art most often look to mRNA expression levels as predictive of the relative protein expression levels. Most importantly, as corroborated by Alberts *et al.*, most genes are, in fact, transcribed into mRNA and translated into protein in direct proportion to their relative mRNA expression levels.

Thus, Applicants submit that due to: (1) the availability of routine methods for generating antibodies; (2) the availability of routine techniques for detecting the presence of specific proteins; (3) the knowledge of the amino acid sequence constituting SEQ ID NO: 310; and (4) the high level of skill in the field of immunology and molecular biology, one

skilled in the art could routinely generate the claimed antibodies and determine whether any given biological samples contained a polypeptide of the invention and satisfy the limitations recited in the claims. Accordingly, Applicants respectfully request that the Examiner withdraw claims 1-75 under 35 U.S.C. § 112, first paragraph.

B. Claims 7, 29, 44, and 67

Claims 7, 29, 44, and 67 (drawn to antibodies that bind proteins that are glycosylated) were rejected under 35 U.S.C. § 112, first paragraph, because allegedly:

> [t]he specification does not teach antibodies that bind carbohydrate moieties and does not provide any working examples to assist one skilled in the art to make antibodies that bind carbohydrate moieties.

See, Paper No. 20040503, page 14, penultimate paragraph.

Applicants respectfully disagree and traverse.

Preliminarily, Applicants point out that claims 7, 29, 44, and 67 are directed to antibodies that bind a native or recombinantly produced protein that happens to be glycosylated and not antibodies that bind carbohydrate moieties of the protein. Accordingly, the specification at page 364, lines 33-37, teaches that the polypeptides of the invention "include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods." Furthermore, the specification also teaches that:

> [p]olypeptides of the present invention, and preferably the secreted form, can also be recovered from natural sources, including bodily fluids, tissues and cells, whether directly isolated or cultured; products of chemical synthetic procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast, higher plant, insect, and mammalian cells in culture. Depending upon the host employed in a recombinant production procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated.

See, specification, page 377, lines 16-23. Further, the specification teaches:

> [a]ntibodies generated against the polypeptides corresponding to a sequence of the present invention can be obtained by direct injection of the polypeptides into an animal or by administering the polypeptides to an animal, preferably a nonhuman. The antibody so obtained will then bind the polypeptides itself.

See, specification, Example 10, page 410.

Hence, the present specification teaches that antibodies can be generated against the polypeptide of the invention whether naturally or synthetically produced. This includes

natural and synthetically produced glycosylated proteins. Furthermore, animal immunization of such glycosylated proteins will result in production of antibodies that bind the glycosylated forms of the injected protein. Generation and production of such antibodies does not require knowledge or identification of the carbohydrate moieties or the epitopes created or hidden by glycosylation. Production of antibodies may be performed in the complete absence of any knowledge pertaining to the particular epitopes which induce antibody binding. Moreover, such methods were routinely performed by those of ordinary skill in the art as of the earliest claimed priority date in the present application. As such, the present specification provides adequate enablement for production of all of the claimed antibodies. Accordingly, it is respectfully requested that the rejection of claims 7, 29, 44, and 67 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

C. Claims 38-75

The Examiner has also rejected claims 38-75 under 35 U.S.C. § 112, first paragraph, because allegedly "the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description." *See* Paper No. 20040503, pages 16-18.

Applicants respectfully point out that the specification, as set forth in 37 C.F.R. § 1.809 (d), clearly describes at page 4, line 34 to page 5, line 6 that ATCC Deposit No. 97975 has been deposited under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure with the following International Depository Authority: American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, Virginia 20110-2209, USA. Thus, Applicants respectfully submit that the specification is in full compliance with 37 C.F.R. §§ 1.801-1.809. However, in accordance with the Examiner's request, the following declaration is respectfully submitted:

Availability of the Deposit

As attorney for the above-identified Applicants in the above-identified patent application, I hereby declare and state that:

> Human Genome Sciences, Inc., the assignee of the present application, has deposited biological material under the terms of the Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purposes of Patent Procedure with the following International Depository Authority: American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia

20110-2209 (present address). The deposit was made on April 4, 1997, accepted by the ATCC, and given ATCC Accession Number 97975. In accordance with M.P.E.P. § 2410.01 and 37 C.F.R. § 1.808, assurance is hereby given that all restrictions on the availability to the public of ATCC Accession Number 97975 will be irrevocably removed upon the grant of a patent based on the instant application, except as permitted under 37 C.F.R. § 1.808(b). The assignee of the present application has been notified of its responsibility to replace the deposited biological material should the deposited material be destroyed or rendered non-viable.

In view of the above affirmation and explanation, attested to by the signature (below) of the Agent for the Applicants, it is respectfully requested that the rejection of claims 38-75 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Conclusion

Applicants respectfully request that the above-made amendments and remarks be entered and made of record in the file history of the instant application. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicant would expedite the examination of this application.

If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425.

Respectfully submitted,

Date: September 29, 2004

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